Hypophosphatasia: To Treat or Not to Treat? A Case Study

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Conflict of Interest Disclosure
None

A conflict of interest exists when an individual is in a position to profit directly or indirectly through application of authority, influence, or knowledge in relation to the affairs of PENS. A conflict of interest also exists if a relative benefits or when the organization is adversely affected in any way.

Case Study
C.P. is a 1yr 11mo old female who was referred by her pediatric dentist for endocrine evaluation associated with premature tooth loss.
History

- 8.5mo: 2 bottom incisors came in
- 10mo: 2 lower teeth laterally came in
- 17mo: 2 central incisors fell out
- 20mo: full set of teeth came in
- 22mo: 2 teeth laterally to her central incisors were pulled due to being loose and fear of aspiration

History continued

- No fractures (despite a fall at age 5wk)
- No developmental delay
- No complaints of bone or muscle pain
- No seizures

Screening labs

- Normal calcium: 10.0ng/dL
- Normal iPTH: 32.4pg/mL (7.5-53.5)
- Low alkaline phosphatase: 58 U/L (129-291)
  Repeat alk phos also low: 76 U/L
- High vitamin B6: 225mcg/L (5-50)
- High urine phosphoethanolamine: 803nmol/mg Cr.

- This confirmed the diagnosis of hypophosphatasia (HPP)
- Of note: skeletal survey was normal
What is Hypophosphatasia

- Potentially life-threatening, systemic, inherited metabolic disorder caused by a loss-of-function mutation in the gene encoding tissue-nonspecific alkaline phosphatase (TNALP)
- The biological hallmark of HPP is low alkaline phosphatase (ALP) activity

Low ALP activity results in accumulation of TNSALP substrates:
- Pyridoxal 5'-phosphate (PLP): major circulating form of vitamin B6
- Inorganic pyrophosphate (PPI): potent inhibitor of mineralization
- Phosphoethanolamine (PEA): diagnostic marker

Categories of HPP

- Perinatal
- Infantile
- Childhood
- Adult
- Odonto
New Treatment

- Asfotase alfa (enzyme-replacement therapy) was FDA approved for treatment of hypophosphatasia in 2015
- Given SQ 3x/wk
- Can cause significant site reactions with lipoatrophy/dystrophy

To Treat or Not to Treat?

Our decision:

- Hold off on treatment
- Currently only symptom is premature tooth loss
- No skeletal manifestations
- No pain or quality of life limitations
- Continued close observation (every 6mo)
- Consider treatment, if it evolves into juvenile HPP with skeletal manifestations and symptoms interfering with quality of life
Questions, Comments, Suggestions?

Thank you